

Please amend the application as follows:

In the Claims

Please cancel claims 78, 79 and 107, amend claims 22, 34, 39, 40, 43, 46, 48, 59, 62, 64, 66, 71, 72, 75, 87, 92, 93, 105, 106, 110, 111, 114, 115 and 116, and add new claim 117 as follows:

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22. (Three Times Amended) A method for detecting a specific target cell in a cell suspension of a mixed cell population, in a fluid system containing a mixed cell population, or in a cell suspension prepared from a solid tissue, with the exception of normal and malignant hematopoietic cells in blood and bone marrow, the method comprising the steps of:

- cl 1
- a. coating paramagnetic particles or beads with a first antibody or antibody fragment directed against a second antibody or antibody fragment;
  - b. incubating the second antibody or antibody fragment with the cell suspension to bind the second antibody or antibody fragment with the target cell, thereby creating a cell mixture, wherein the second antibody or antibody fragment is directed against a membrane structure specifically expressed on the target cell and not on a non-target cell in the cell mixture;
  - c. washing the cell mixture to remove unbound second antibody or antibody fragment;
  - d. mixing the coated paramagnetic particles or beads with the washed cell mixture;
  - e. incubating the washed cell mixture and the coated paramagnetic particles under gentle rotation at about 4°C until target cell-bead rosettes are formed; and
  - f. visually detecting the target cell-bead rosettes after incubation.
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34. (Amended) The method of claim 22, wherein the second antibody or fragment thereof is directed against an antigen or a receptor in a cell with abnormal developmental patterns.

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el3 39. (Amended) The method of claim 22, wherein the second antibody or antibody fragment is directed against fibronectin receptor,  $\beta$ -integrin, vitronectin receptor,  $\alpha\beta$ 3-integrin, P-selectin including GMP-140, CD44-variants, N-CAM including CD-56, E-cadherin, Le<sup>x</sup>, carcinoembryonic antigen or CEA, EGF receptor, c-erbB-2 including HER2, transferin receptor, TNF-receptor, molecular weight antigen, p95-100, sarcoma antigens including TP-1 and TP-3 epitope, Mv 200kD, Mv160kD, MOC-31 epitope including cluster 2 epithelial antigen, MUC-1 antigen including DF3-epitope and gp290kD, prostate molecular antigen, TAG 72, bladder carcinoma antigen, Mv 48kD colorectal carcinoma antigen, lung carcinoma antigen Mv 350-420kD, Mel-14 epitope,  $\beta_2$ -microglobulin, Apo-1 epitope, or pan-human cell antigen.

el4 40. (Amended) The method of claim 22, wherein the second antibody or antibody fragment is directed against a growth factor receptor or an oncogene product expressed on the membrane of a malignant cell.

el5 43. (Amended) The method of claim 34, wherein the second antibody or antibody fragment is directed against breast, ovarian or lung carcinoma cells; melanoma, sarcoma, glioblastoma or cancer cells of the gastrointestinal tract; melanoma, sarcoma, glioblastoma or cancer cells of the genitourinary tract; or melanoma, sarcoma, glioblastoma or cancer cells of the reticuloendothelial system.

el6 46. (Three Times Amended) A kit for performing the method of claim 22, the kit comprising:

a. a first antibody, wherein said first antibody is a specific monoclonal antibody or antibody fragment directed against a second antibody or antibody fragment, said first antibody capable of coating a paramagnetic particle or bead without removing its antigen-binding ability;

b. a paramagnetic particle or bead; and

c. a second antibody, wherein said second antibody is a specific monoclonal antibody or antibody fragment directed against an antigen or a receptor within or on the target cell;

wherein said second antibody or antibody fragment is conjugated to a detectable label.

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48. (Four Times Amended) A method for detecting a specific target cell in a cell suspension of a mixed cell population, in a fluid system containing a mixed cell population, or in a cell suspension prepared from a solid tissue, with the exception of normal and malignant hematopoietic cells in blood and bone marrow, the method comprising the steps of:

- a. coating paramagnetic particles or beads with a first antibody directed against a second antibody or antibody fragment;
- b. incubating the second antibody or antibody fragment with the cell suspension to bind the second antibody or antibody fragment with the target cell, thereby creating a cell mixture, wherein the second antibody or antibody fragment is directed against a membrane structure specifically expressed on the target cell and not on a non-target cell in the cell mixture;
- c. washing the cell mixture to remove unbound second antibody or antibody fragment;
- d. mixing the coated paramagnetic particles with the washed cell mixture;
- e. incubating the washed cell mixture and coated paramagnetic particles under gentle rotation at about 4°C until target cell-bead rosettes are formed; and
- f. visually detecting the target cell-bead rosettes.

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59. (Amended) The method of claim 48, wherein the second antibody or antibody fragment directed against a membrane structure specifically expressed on the target-cell is a murine or a human antibody or fragment thereof.

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62. (Three Times Amended) The method of claim 48, wherein when the ratio of target cell/total cells in the cell mixture is  $\leq 1\%$ , the method further comprises after incubating, applying a magnetic field to separate out the target cell-bead rosettes.

cl10 64. (Amended) The method of claim 48, wherein visually detecting includes counting the target cell-bead rosettes using a microscope or a cell or particle counting device.

cl11 66. (Amended) The method of claim 48, wherein the second antibody or fragment thereof is directed against an antigen or a receptor in a cell with abnormal developmental patterns.

cl12 71. (Amended) The method of claim 48, wherein the second antibody or antibody fragment is directed against fibronectin receptor,  $\beta$ -integrin, vitronectin receptor,  $\alpha\gamma\beta 3$ -integrin, P-selectin, GMP-140, CD44-variants, N-CAM, E-cadherin, Le<sup>y</sup>, CEA, EGF receptor, c-erbB-2, HER2, transferin receptor, TNF-receptor, high molecular weight antigen, p95-100, TP-1 and TP-3 epitope, Mv 200kD, Mv160kD, MOC-31 epitope, cluster 2 epithelial antigen, MUC-1 antigen, DF3-epitope, gp290kD, prostate high molecular antigen, TAG 72, bladder carcinoma antigen, Mv 48kD colorectal carcinoma antigen, lung carcinoma antigen Mv 350-420kD, Mel-14 epitope,  $\beta_2$ -microglobulin, Apo-1 epitope, or pan-human cell antigen.

cl13 72. (Amended) The method of claim 48, wherein the second antibody or antibody fragment is directed against a growth factor receptor or an oncogene product expressed on the membrane of a malignant cell.

cl14 75. (Amended) The method of claim 66, wherein the second antibody or antibody fragment is directed against breast, ovarian or lung carcinoma cells; melanoma, sarcoma, glioblastoma or cancer cells of the gastrointestinal tract; melanoma, sarcoma, glioblastoma or cancer cells of the genitourinary tract; or melanoma, sarcoma, glioblastoma or cancer cells of the reticuloendothelial system.

cl15 87. (Two Times Amended) A method for detecting tumor cells in a cell suspension of mixed cell population or in a cell suspension prepared from a solid tissue, with the

exception of normal and malignant hematopoietic cells in blood and bone marrow, comprising:

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- a) coating paramagnetic particles with a first antibody or fragment directed against a second tumor-specific monoclonal antibody or fragment;
  - b) incubating the second tumor specific antibody with the cell suspension to allow the second tumor specific antibody to bind the tumor cells;
  - c) washing the cell suspension to remove unbound second antibody or antibody fragment;
  - d) mixing the coated paramagnetic particles with the cell suspension;
  - e) incubating the mixture at about 4°C under gentle rotation until tumor cell-bead rosettes are formed; and
  - f) visually detecting the tumor cell-bead rosettes.
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92. (Amended) A method of detecting metastatic cancer cells in a suspension of a mixed cell population or in a single cell suspension from a solid tissue when the metastatic cancer cells are present at less than 1% of the cell suspension, the method comprising the steps of:

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- a) coating paramagnetic particles with a first antibody or fragment thereof directed against a second cancer-specific monoclonal antibody or fragment;
  - b) incubating the second cancer-specific antibody with the cell suspension to allow the second cancer-specific antibody to bind the cancer cells;
  - c) washing the cell suspension to remove unbound second antibody or antibody fragment;
  - d) mixing the coated paramagnetic particles or beads with the cell suspension;
  - e) incubating the mixture under gentle rotation at about 4°C until cancer cell-bead rosettes are formed;
  - f) applying a magnetic field to separate out the cancer cell-bead rosettes; and
  - g) visually detecting the cancer cell-bead rosettes.
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93. (Amended) A method according to claim 92, wherein the cancer-specific monoclonal antibody is specific for cancer antigens comprising a growth factor receptor, an oncogene product expressed on the membrane of a malignant cell, an adhesion membrane molecule, an MDR protein, breast, ovarian or lung carcinoma cells; melanoma, sarcoma, glioblastoma or cancer cells of the gastrointestinal tract; melanoma, sarcoma, glioblastoma or cancer cells of the genitourinary tract; or melanoma, sarcoma, glioblastoma or cancer cells of the reticuloendothelial system.

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105. (Amended) The method of claim 22, wherein visually detecting includes counting the target bead rosettes using a microscope or a cell or particle counting device.

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106. (Amended) The kit of claim 46, comprising a paramagnetic particle or bead coated with the first antibody and a paramagnetic particle or bead not coated with antibody.

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110. (Once Amended) The method according to claim 22, wherein the target cells are detected at a sensitivity of one target cell per 1000 or more total cells.

111. (Amended) The method according to claim 22, wherein the second antibody is an IgG antibody and the first antibody recognizes the Fc-portion of the second antibody.

114. (Once Amended) The method according to claim 48, wherein the target cells are detected at a sensitivity of one target cell per 1000 or more total cells.

cl21  
115. (Amended) The method according to claim 48, wherein the second antibody is an IgG antibody and the first antibody recognizes the Fc-portion of the second antibody.

116. (Once Amended) The method according to claim 87, wherein the target cells are detected at a sensitivity of one target cell per 1000 or more total cells.

117. (New) A kit for performing the method of claim 22, the kit comprising:

a. a first antibody, wherein said first antibody is a specific monoclonal antibody or antibody fragment directed against a second antibody or antibody fragment, said first antibody capable of coating a paramagnetic particle or bead without removing its antigen-binding ability;

b. a paramagnetic particle or bead; and

c. a second antibody, wherein said second antibody is a specific monoclonal antibody or antibody fragment directed against an antigen or a receptor within or on the target cell, wherein the second antibody or antibody fragment is directed against fibronectin receptor,  $\beta$ -integrin, vitronectin receptor,  $\alpha\gamma\beta 3$ -integrin, P-selectin including GMP-140, CD44-variants, N-CAM including CD-56, E-cadherin, Le<sup>y</sup>, carcinoembryonic antigen or CEA, EGF receptor, c-erbB-2 including HER2, transferin receptor, TNF-receptor, molecular weight antigen, p95-100, sarcoma antigens including TP-1 and TP-3 epitope, Mv 200kD, Mv160kD, MOC-31 epitope including cluster 2 epithelial antigen, MUC-1 antigen including DF3-epitope and gp290kD, prostate molecular antigen, TAG 72, bladder carcinoma antigen, Mv 48kD colorectal carcinoma antigen, lung carcinoma antigen Mv 350-420kD, Mel-14 epitope,  $\beta_2$ -microglobulin, Apo-1 epitope, or pan-human cell antigen;

wherein said second antibody or antibody fragment is conjugated to a detectable label.

Please cancel claims 78, 79, and 107.